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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,497	10/11/2000	Richard F Selden	10278-022001	5761

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EXAMINER
NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/686,497	Applicant(s) Selden et al.
	Examiner Nashaat T. Nashed	Art Unit 1652

-- ***The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 26, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) *16-25* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Oct 11, 2000* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4 & 12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, claims 1-15 in Paper No. 11 is acknowledged.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicants are required to comply with the sequence rule by filing a new sequence listing, CRF, and an amendment to delete the paper copy of the sequence listing and enter the new one along with a statement indicating that the CRF and the paper copy of the sequence listing are identical and contain no new matter.

The disclosure is objected to because of the following informalities: the disclosure contains numerous reference to nucleic acid from GenBank with accession numbers. Since the data base can change the accession numbers of any deposited sequences without prior notification, or cross reference the old accession numbers to a new accession numbers, the reference to data base accession number is improper. Applicant must incorporate the sequences into the specification by filing a new sequence listing in paper and computer readable forms containing the nucleic/amino acid sequences identified by sequence identification numbers along with statement indicating that both sequence listing are identical and contain no new matter. Furthermore, the specification must be amended to replace the reference to accession numbers and data bases with sequence identification numbers only. In addition, page 33, line 3 from the bottom, an amino acid sequence is not identified with a sequence identification number.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "non-common codon", "less-common codon" and "common codon" in claims 1-15 are relative terms which renders the claim indefinite. The term "non-common codon", "less-common codon" and "common codon" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised

of the scope of the invention. It is note that the applicants have attempted to define the phrases on page 21 in the light of Table 1 which shows the preferred codon for human. While the three phrases are self explanatory in some cases such as for Leu wherein the CTG is a common-codon with 58%, CTC is the less common-codon with 26% and followed with the non-common codon with 3 and 5% for CTA and CTT. In contrast, Lys has only two codon, AAA with 18% of the time and AAG with 82% of the time. The question here becomes is 18% frequent enough to be less common-codon? or not sufficiently common enough to be non-common codon?, see other example in table 1 for Cys, Gln, Glu, His, Lys, and Phe among others. Even when there are more than one codon for amino acids the differences between non-common and less common can be difficult to distinguish. For example, Thr has four codon. The most abundant is the ACC with 57% of the occurance in human, leaving the three other with equal chances of occurance at 14, 14 and 15%, see also Pro and Ala.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64-135 of copending Application No. 09/407,605 ('605). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 64-79 and 113-135 of the '605 application are generic claims drawn to a modified nucleic acid sequence of a protein in which non-common and less common codons are replaced with common codons, method of preparing said nucleic acid, and mammalian cells transformed with said nucleic acid. Claims 1-15 of the instant application are essentially the same claims except that they are drawn to nucleic acid encoding α-galactosidase and the codons are not

limited to a particular biological species. Claims 80-112 of the copending '605 application are drawn to a modified nucleic acid by replacing non-common and less common codon by a common codon wherein the modified nucleic acid encodes factor XIII and IX. The claims of the instant application are obvious variants of specific embodiments of claims 80-112 in view of Bishop *et al.* and Morgan *et al.* who teach that gene encoding human α-galactosidase A and its relationship to Fabry disease. Such a teaching would provide motivation to one of ordinary skill in the art to develop a recombinant method to make the human enzyme in large quantities, see bellow. If the generic claims 64-79 and 113-135 are patented the embodiment of the instant claims would be cover by the generic claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seed (IDS (paper number 12): Ref. AG: WO 96/09378) in view of the prior art as exemplified by Kim *et al.* [IDS (paper number 4): Ref AQ: Gene 199, 293-301 (1997)], Morgan *et al.* [Pediatr. Nephrol. (1987) 1, 536-539], Bishop *et al.* (Proc. Natl. Acad. Sci. U. S. A. 83, 4859-4863), and [Nucleic Acid Research 20, 2111-2118 (1992)].

Seed teaches a synthetic mammalian gene in which at least one non-preferred or less preferred codon is replaced with a mammalian preferred codon, see page 1, line 20-26. The preferred codons are taught on page 1, lines 27-32. He teaches that said modified mammalian gene is expressed at much higher level which is 110%, 150%, 200%,

500%, 1000% or 10,000% relative to that of the wild-type mammalian gene, see page 2, lines 10-16. Also, he teaches a method of preparing the nucleic acid in which the non-preferred or less preferred codon are identified in a natural gene and replaced by a preferred codon encoding the same amino acid, see page 3, lines 8-14. The mammalian gene could encode any desired protein or fragment thereof having any length, see page 4, line 3-9. Seed does not teach a synthetic gene encoding α-galactosidase.

Kim *et al.* teach that selective codons in a given gene positively correlate with its expression efficiency, see abstract. Also, they teach the codon optimization of a leader sequence leads to further enhancement of a synthetic gene, see page 297, right column, section 3.3.

Morgan *et al.* teach that Anderson-Fabry disease is an X-linked lysosomal storage disorder due to α-galactosidase A deficiency, see abstract.

Bishop *et al.* teach the cDNA encoding human α-galactosidase A, see Figure 2, and that mutation in the DNA encoding the enzyme causes Fabry disease, see the paragraph bridging the left and right columns on page 4859.

Wada *et al.* teach the common codon used by many organisms.

Morgan *et al.* provides one of ordinary skill in the art with motivation to develop a method for making α-galactosidase to use for the treatment of Anderson-Fabry disease as they teach Anderson-Fabry disease is caused by deficiency in human α-galactosidase A. Seed and Kim further motivate the ordinary skill in the art to synthesize α-galactosidase in which the non-common and less common codons are replaced with common codon for mammalian cells to enhance the expression of α-galactosidase A in said cells. Thus, it would have been obvious to one of ordinary skill in the art to identify the less-common and non-common codon used for mammalian cells in a gene encoding α-galactosidase such as the human α-galactosidase A taught by Bishop *et al.* (12-15), synthesize the codon optimized gene (claims 1-8), construct a mammalian expression vectors comprising the synthetic gene (claim 9), transform a mammalian cell with said vector (claim 10), and express the synthetic gene in a mammalian cell of choice as taught by Seed and Kim *et al.* to make the desired α-galactosidase (claim 11). It should be noted that the ordinary skill in the art would have been motivated to change every single less common and non-common codon to a common codon to optimize the level of expression of the desired α-galactosidase in the host cell so the resulting sequence could be 100% common codons (claims 1-8). Also, applicants should note that any α-galactosidase gene from any biological source can be optimized for express in almost any host cell including human, *E. coli*, yeast, and insect among others because the common codons for many organisms are known, see Wada *et al.* Thus, the claimed invention was within the ordinary

skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner